REMARKS

Claims 1-9 are pending in the instant application. With this Amendment, Claims 1, 2 and 4 are canceled without prejudice, new Claims 10-13 are added and Claims 3 and 5 are amended. Thus, after entry of the present Amendment, Claims 3 and 5-13 are pending in the present application. For the PTO's convenience, a clean copy of pending Claims 3 and 5-13 are attached hereto as Exhibit B.

I. THE AMENDMENT TO THE CLAIMS

Applicants have canceled Claims 1, 2 and 4 without prejudice, and Applicants have amended Claims 3 and 5 to correct minor errors in claim language and to conform with the election of SEQ ID NOS:9-18 for prosecution on their merits.

Applicants have added new Claims 10-13. New Claims 10-13 are fully supported by the specification and claims as originally filed. For instance, new Claims 10-12 are supported in the specification, for example, at page 16, lines 5-10, and by original Claim 1. New Claim 13 is supported in the specification, for example, at page 16, line 26, through page 17, line 4, and at page 13, line 7, through page 14, line 2.

As the amendments are fully supported by the specification and claims as originally filed, they do not constitute new matter. Entry thereof is respectfully requested.

II. SEQ ID ELECTION

Applicants hereby elect SEQ ID NOS:9-18 for prosecution on their merits. Applicants have amended Claims 3 and 5 to conform with this election.

III. OBJECTION TO CLAIM 5

Claim 5 has been objected to because the term "GTS" is defined in the specification but allegedly not defined in the claims. Although one of skill in the art would readily understand Claim 5 when read in light of the specification, in order to expedite prosecution Applicants have amended Claim 5 to recite "gene trapped sequence" as recommended by the PTO.

IV. THE REJECTION UNDER 35 U.S.C. § 101 (SUBJECT MATTER)

Claim 1 stands rejected because the subject matter of Claim 1 is allegedly non-statutory. The PTO asserts that the recited oligonucleotide is an unaltered product of nature. As Claim 1 has been canceled, Applicants submit that the rejection under 35 U.S.C. § 101 is moot and request that it be withdrawn. Applicants submit that new Claims 10-13 meet the requirements for patentability under 35 U.S.C. § 101.

V. THE REJECTION UNDER 35 U.S.C. § 101 (UTILITY)

Claims 1-4 stand rejected under 35 U.S.C. § 101 as allegedly lacking patentable utility. Applicants note that Claims 1, 2 and 4 have been canceled without prejudice with the present Amendment. Applicants respectfully traverse the rejection on the ground that Claim 3 is patentably useful.

According to 35 U.S.C. § 101, whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter may obtain a patent therefor subject to the conditions and requirements of 35 U.S.C. The threshold of utility is not high. *Juicy Whip Inc. v. Orange Bang Inc.*, 51 USPQ2d 1700, 1702 (Fed. Cir. 1999). An invention is "useful" under 35 U.S.C. § 101 if it is capable of providing some identifiable benefit. *Id.* (*citing Brenner v. Manson*, 383 U.S. 519, 534, 148 USPQ 689, 695 (1966)).

Claim 3 and new Claims 10-13 recite isolated polynucleotides corresponding to SEQ ID NOS:9-18. Such polynucleotides have tremendous identifiable benefits.

For instance, the claimed polynucleotides can be used to expand the utility of current genomic data such as human genomic data. Persons of skill in the art readily recognize the utility, both scientific and commercial, of genomic data from species such as humans and mice. For example, billions of dollars have been invested in the human genome project resulting in useful human genomic data. *See, e.g.*, Venter *et al.*, 2001, Science 291:1304. The results have been a stunning success as the utility of human genomic data has been widely recognized as a great gift to humanity. *See, e.g.*, Jasny and Kennedy, 2001, Science 291:1153. Technology that enhances the utility of useful genomic data is itself useful.

Current genomic data lacks necessary information that would make the data even more useful. For instance, of the myriad putative genes identified by the Human Genome Project, only a relatively small number are known to be expressed. Current technology

struggles to separate expressed genes from "junk" DNA in the putative genes identified by massive sequencing efforts.

As disclosed in the specification at pages 1-2, isolated expressed DNA sequences from the human genome have tremendous utility in identifying the expressed genes in raw genomic sequences. Furthermore, the gene trapped sequences of the present invention overcome some of the limitations of conventional cDNA and expressed sequence tag libraries. In particular, the gene trapped sequences of the present invention, including SEQ ID NOS:9-18, were identified using reverse orientation retroviral gene trap vectors that nonspecifically integrate into the target cell genome. These gene trap vectors do not rely solely on the degree of endogenous mRNA expression of a gene for identification of that gene. Hence, the gene trap vectors are able to trap even poorly expressed genes. The identification of gene trapped sequences such as SEQ ID NOS:9-18 thus increases the value and utility of raw genomic data by enabling the identification of expressed genes, even poorly expressed genes, within the genomic data.

Furthermore, the specification provides numerous other credible, specific and substantial utilities for polynucleotides comprising SEQ ID NOS:9-18. For example, polynucleotides comprising SEQ ID NOS:9-18 can be used for diagnostic gene expression and analysis, for cross species hybridization analysis, antisense inhibition, gene targeting, identifying exon splice junctions, gene therapy, gene delivery and chromosome mapping. Each of these utilities is credible, specific and substantial.

For instance, at page 8, lines 14-21, the specification describes the utility of polynucleotides comprising SEQ ID NOS:9-18 for physical and genetic mapping of the human genome and/or the genome of model organisms. To illustrate, early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. Giemsa staining, however, suffered from limited resolution. In particular, the human genome could only be divided into as many as 350 to 850 bands by conventional Giemsa staining techniques. The effective resolution of genetic maps based on such techniques was limited to about 5 to 10 megabases.

Hybridization techniques such as fluorescence in situ hybridization revolutionized genetic mapping techniques. With such hybridization techniques the resolution of genetic mapping techniques can be improved to resolutions of about 50 kilobases to 100 kilobases or even greater. However, such mapping techniques based on hybridization require specific

hybridization probes in order to be effective. Polynucleotides comprising SEQ ID NOS:9-18 provide additional specific probes that can be used to improve the utility of current genetic mapping techniques. Since the use of a polynucleotide comprising one of SEQ ID NOS:9-18 for mapping specifically identifies the genomic location corresponding to the polynucleotide, the use is specific for the polynucleotide.

Since polynucleotides comprising SEQ ID NOS:9-18 can be used to expand the utility of genomic data, to expand the utility of current mapping techniques and for the other utilities discussed above and in the specification, Applicants submit such polynucleotides satisfy the requirements for patentability under 35 U.S.C. § 101. Applicants therefore respectfully request that the rejection of Claim 3 under 35 U.S.C. § 101 be withdrawn. Applicants also submit that new Claims 10-13 meet the requirements for patentability under 35 U.S.C. § 101.

VI. REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH (UTILITY)

Claims 1-4 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking utility. Applicants note that Claims 1, 2 and 4 have been canceled without prejudice with the present Amendment. Applicants traverse this rejection on the ground that Claim 3 has significant patentable utility as discussed in Section V, above. Applicants respectfully request that the rejection of Claim 3 under 35 U.S.C. § 112, first paragraph, be withdrawn. Applicants also submit that new Claims 10-13 meet the requirements for patentability under 35 U.S.C. § 112, first paragraph.

VII. REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, (WRITTEN DESCRIPTION)

Claims 1, 3 and 4 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification. Applicants note that Claims 1 and 4 have been canceled without prejudice with the present Amendment. Applicants traverse this rejection on the ground that amended Claim 3 is fully supported by the specification and claims as originally filed.

35 U.S.C. § 112, first paragraph, requires that the specification contain a written description of the invention. An applicant must convey with reasonably clarity to those skilled in the art that the applicant was in possession of the invention. *Vas-Cath v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). An adequate description of a chemical genus requires a precise definition by *structure, formula, chemical name* or *physical properties* sufficient to distinguish the genus from other materials. *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). The standard for claims involving chemical materials has been explicitly stated by the Federal Circuit:

> In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. *Univ. of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

However, description of the function of genetic material is not an adequate description of the genetic material:

> In claims to genetic material...a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. *Id.*

Thus, a claim describing a genus of nucleic acid by *structure, formula, chemical name* or *physical properties* sufficient to distinguish the genus from other materials meets the written description requirement of 35 U.S.C. § 112, first paragraph, as elaborated by the Federal Circuit in *Fiers v. Revel* and in *Univ. of California v. Eli Lilly and Co.*

Claims 3 and 10-13 recite isolated polynucleotides corresponding to at least one of SEQ ID NOS:9-18. The isolated polynucleotides are fully described by *structure* or by *physical properties*, or both, sufficient to distinguish the claimed isolated polynucleotides from other materials.

For instance, Claim 3 recites an isolated polynucleotide that comprises a contiguous stretch of at least about 60 nucleotides of at least one of SEQ ID NOS:9, 12-14, 16-18. Given the description of Claim 3, one of skill in the art can readily distinguish the isolated polynucleotides of Claim 3 from other materials by the *structural* description of Claim 3. If an isolated polynucleotide comprises a contiguous stretch of at least about 15 nucleotides of at least one of SEQ ID NOS:9, 12-14, 16-18, the isolated polynucleotide is within the genus of Claim 3. Other chemical materials that lack this *structural* feature are not within the genus. Claims 10-12 similarly recite genera of isolated polynucleotides with precise *structural* definitions of chemical genera.

New Claim 13 recites an isolated polynucleotide capable of hybridizing to a polynucleotide of Claim 3, 10 or 11. New Claim 13 describes a genus of polynucleotides by a *physical property* that readily distinguishes the claimed polynucleotides from other materials. In particular, those polynucleotides with the *physical property* of being capable of hybridizing to a polynucleotide of Claim 3, 10 or 11 are within the genus of Claim 13. Other chemical materials that lack this *physical property* are not within the genus. One of skill in the art can readily distinguish the polynucleotides of Claim 13 from other materials. New Claim 13 thus meets the written description requirement.

Since Claim 3 meets the written description requirement, Applicants respectfully request that the rejection of Claims 3 under 35 U.S.C. § 112, first paragraph, be withdrawn. Applicants also submit that new Claims 10-13 meet the requirements for patentability under 35 U.S.C. § 112.

VIII. THE REJECTIONS UNDER 35 U.S.C. § 102(b)

Claims 1-3 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by at least one of several references. Claim 1 stands rejected as allegedly being anticipated by Bredt et al., 1991, Nature 351:714-718 ("Bredt"); by EST Accession No. AI797618, 1997 ("AI797618"); by Pearce, 1998, GENEMBL Accession No. HS127D3 ("Pearce"); by Hillier et al., 1995, EST Accession No. R91187 ("Hillier"); by Gray et al., 1998, GENEMBL

Accession No. AC004499 ("Gray"); by Feng et al., 1997, EST Accession No. B21891 ("Feng"); by Zhao et al., 1997, EST Accession No. AQ416115 ("Zhao AQ416115") by Hoof et al., 1992, Nucleic Acids Res. 20:5475 ("Hoof"); by Chu et al., 1993, Nucleic Acids Res. 21:1672 ("Chu"); by Saha et al., 1993, Gene 132:285-289 ("Saha"); by Lennard et al., 1997, GENEMBL Accession No. CEVZC374L ("Lennard"); or by Emmenegger et al., 1996, GENEMBL Accession No. U50402 ("Emmenegger"). Claims 1 and 3 stand rejected as allegedly anticipated by Zhao et al., 1997, EST Accession No. AQ344286 ("Zhao AQ344286"). Claims 1-3 stand rejected as allegedly anticipated by Waterson et al., 1998, GENEMBL Accession No. AC005061 ("Waterson"); by EST Accession No. AW241926, 1997 ("AW241926"); or by EST Accession No. AI47895 ("AI47895"). Since Claims 1 and 2 have been canceled without prejudice, Applicants submit that the rejections of Claims 1 and 2 are moot. Applicants traverse the rejections of Claim 3 on the ground that none of the references cited by the PTO teach or suggest each and every element of amended Claim 3.

The standard for anticipation under 35 U.S.C. §102 is strict identity. Anticipation under § 102 can only be established by a single prior art reference that teaches each and every element of the claimed invention. *Structural Rubber Products Co. v. Park Rubber Co.* 223 USPQ 1264 (1984).

Amended Claim 3 recites an isolated polynucleotide comprising a contiguous stretch of at least about 60 nucleotides of at least one of SEQ ID NOS:9, 12-14, 16-18. Claim 10 recites an isolated polynucleotide that comprises at least about 30 nucleotides of SEQ ID NOS:9, 13, 14, 17 18. Claim 11 recites an isolated polynucleotide that comprises at least about 40 nucleotides of SEQ ID NOS:9, 12-14, 16-18. Claim 12 recites an isolated polynucleotide that comprises at least one of SEQ ID NOS:9-18. Claim 13 recites an isolated polynucleotide is capable of hybridizing to a polynucleotide of Claim 3, 10 or 11.

Bredt does not teach or suggest each and every element of amended Claim 3 or new Claims 10-14. The PTO asserts that Bredt teaches an oligonucleotide comprising a contiguous stretch of 21 bases of SEQ ID NO:9. However, Bredt does not teach or suggest an isolated polynucleotide comprising a contiguous stretch of at least about 30 nucleotides of at least one of SEQ ID NO:9. As such, Bredt does not teach or suggest each and every element of Claims 3 or 10-14.

AI797618 does not teach or suggest each and every element of amended Claim 3 or new Claims 10-14. The PTO asserts that AI797618 teaches an oligonucleotide comprising a

contiguous stretch of 21 bases of SEQ ID NO:9. However, AI797618 does not teach or suggest an isolated polynucleotide comprising a contiguous stretch of at least about 30 nucleotides of at least one of SEQ ID NO:9. As such, AI797618 does not teach or suggest each and every element of Claims 3 or 10-14.

Zhao AQ344286 does not teach or suggest each and every element of amended Claim 3 or new Claims 10-14. The PTO asserts that Zhao AQ344286 teaches an oligonucleotide comprising a contiguous stretch of 85 bases of SEQ ID NO:10. However, Zhao AQ344286 does not teach or suggest an isolated polynucleotide comprising SEQ ID NO:10. As such, Zhao AQ344286 does not teach or suggest each and every element of Claims 3 or 10-14.

Waterson does not teach or suggest each and every element of amended Claim 3 or new Claims 10-14. The PTO asserts that Waterson teaches an oligonucleotide comprising a contiguous stretch of 389 bases of SEQ ID NO:11. However, Waterson does not teach or suggest an isolated polynucleotide comprising SEQ ID NO:11. As such, Waterson does not teach or suggest each and every element of Claims 3 or 10-14.

AW241926 does not teach or suggest each and every element of amended Claim 3 or new Claims 10-14. The PTO asserts that AW241926 teaches an oligonucleotide comprising a contiguous stretch of 69, 67 or 43 bases of SEQ ID NO:11. However, AW241926 does not teach or suggest an isolated polynucleotide comprising SEQ ID NO:11. As such, AW241926 does not teach or suggest each and every element of Claims 3 or 10-14.

Pearce or Hillier does not teach or suggest each and every element of amended Claim 3 or new Claims 10-14. The PTO asserts that Pearce or Hillier teaches an oligonucleotide comprising a contiguous stretch of 35 bases of SEQ ID NO:12. However, Pearce or Hillier does not teach or suggest an isolated polynucleotide comprising a contiguous stretch of at least about 40 nucleotides of at least one of SEQ ID NO:12. As such, Pearce or Hillier does not teach or suggest each and every element of Claims 3 or 10-14.

Gray does not teach or suggest each and every element of amended Claim 3 or new Claims 10-14. The PTO asserts that Gray teaches an oligonucleotide comprising a contiguous stretch of 19 bases of SEQ ID NO:13. However, Gray does not teach or suggest an isolated polynucleotide comprising a contiguous stretch of at least about 30 nucleotides of at least one of SEQ ID NO:13. As such, Gray does not teach or suggest each and every element of Claims 3 or 10-14.

Feng does not teach or suggest each and every element of amended Claim 3 or new Claims 10-14. The PTO asserts that Feng teaches an oligonucleotide comprising a contiguous stretch of 21 bases of SEQ ID NO:13. However, Feng does not teach or suggest an isolated polynucleotide comprising a contiguous stretch of at least about 30 nucleotides of at least one of SEQ ID NO:13. As such, Gray does not teach or suggest each and every element of Claims 3 or 10-14.

Zhao AQ416115 does not teach or suggest each and every element of amended Claim 3 or new Claims 10-14. The PTO asserts that Zhao AQ416115 teaches an oligonucleotide comprising a contiguous stretch of 20 bases of SEQ ID NO:14. However, Zhao AQ416115 does not teach or suggest an isolated polynucleotide comprising a contiguous stretch of at least about 30 nucleotides of at least one of SEQ ID NO:14. As such, Zhao AQ416115 does not teach or suggest each and every element of Claims 3 or 10-14.

AI47895 does not teach or suggest each and every element of amended Claim 3 or new Claims 10-14. The PTO asserts that AI47895 teaches an oligonucleotide comprising a contiguous stretch of 122 bases of SEQ ID NO:15. However, AI47895 does not teach or suggest an isolated polynucleotide comprising SEQ ID NO:15. As such, AI47895 does not teach or suggest each and every element of Claims 3 or 10-14.

Hoof, Chu or Saha does not teach or suggest each and every element of amended Claim 3 or new Claims 10-14. The PTO asserts that Hoof, Chu or Saha teaches an oligonucleotide comprising a contiguous stretch of 29 bases of SEQ ID NO:16. However, Hoof, Chu or Saha does not teach or suggest an isolated polynucleotide comprising a contiguous stretch of at least about 40 nucleotides of at least one of SEQ ID NO:16. As such, Hoof, Chu or Saha does not teach or suggest each and every element of Claims 3 or 10-14.

Lennard does not teach or suggest each and every element of amended Claim 3 or new Claims 10-14. The PTO asserts that Lennard teaches an oligonucleotide comprising a contiguous stretch of 19 bases of SEQ ID NO:17. However, Lennard does not teach or suggest an isolated polynucleotide comprising a contiguous stretch of at least about 30 nucleotides of at least one of SEQ ID NO:17. As such, Lennard does not teach or suggest each and every element of Claims 3 or 10-14.

Finally, Emmenegger does not teach or suggest each and every element of amended Claim 3 or new Claims 10-14. The PTO asserts that Emmenegger teaches an oligonucleotide comprising a contiguous stretch of 20 bases of SEQ ID NO:18. However, Emmenegger does

not teach or suggest an isolated polynucleotide comprising a contiguous stretch of at least about 30 nucleotides of at least one of SEQ ID NO:18. As such, Lennard does not teach or suggest each and every element of Claims 3 or 10-14.

Since Bredt, AI797618, Zhao AQ344286, Waterson, AW241926, Pearce, Hillier, Gray, Feng, Zhao AQ416115, AI47895, Hoof, Chu, Saha, Lennard or Emmenegger, alone or in any combination, do not teach or suggest each and every element of amended Claim 3, these references do not anticipate Claim 3. Applicants request that the rejections of Claim 1 under 35 U.S.C. § 102(b) be withdrawn. In addition, Applicants submit that new Claims 10-13 meet the requirements for patentability under 35 U.S.C. § 102(b).

IX. THE REJECTIONS UNDER 35 U.S.C. § 103

Claims 5, 6 and 8 stand rejected under 35 USC § 103(a) as allegedly being unpatentable over a combination of AW241926 or AI147895 in view of Sambrook et al., 1989, Molecular Cloning, pp. 14.2-14.7 ("Sambrook"). Claims 5, 7 and 9 stand rejected over a combination of Sambrook in view of Waterson. The rejections are respectfully traversed on the ground that the references cited by the PTO are not sufficient to establish a *prima facie* case of obviousness against Claims 5-9.

A. The Legal Standard of *Prima Facie* Obviousness

To reject claims in an application under 35 U.S.C. § 103, the Patent Office bears the initial burden of establishing a *prima facie* case of obviousness. *In re Bell*, 26 USPQ2d 1529, 1530 (Fed. Cir. 1993); MPEP § 2142. In the absence of establishing a proper *prima facie* case of obviousness, applicants who comply with the other statutory requirements are entitled to a patent. *In re Oetiker*, 24 USPQ2d. 1443, 1444 (Fed. Cir. 1992). In order to establish *prima facie* obviousness, three basic criteria must be met.

First, the prior art must provide one of ordinary skill in the art with a suggestion or motivation to modify or combine the teachings of the references relied upon by the PTO to arrive at the claimed invention. When an obviousness determination relies on one reference, there must be suggestion or motivation to modify the teaching of the reference in the manner suggested by the PTO. *In re Grabiak*, 226 USPQ 870 (Fed. Cir. 1985). Alternatively, when an obviousness determination relies on a combination of two or more references, there must be some suggestion or motivation to combine the references. *WMS Gaming Inc. v.*

International Game Technology, 51 USPQ2d 1385, 1397 (Fed. Cir. 1999). The suggestion or motivation to combine the references generally arises in the references themselves, but may also be inferred from the nature of the problem or occasionally from the knowledge of those of ordinary skill in the art. *See id.* The mere fact that references *could* be modified or combined does not render the resultant modification or combination obvious unless the prior art also suggests the desirability of the modification or combination. *In re Mills*, 16 USPQ2d 1430 (Fed. Cir. 1990); MPEP § 2143.01.

Second, the prior art must provide one of ordinary skill in the art with a reasonable expectation of success. Thus, the skilled artisan, in light of the teachings of the prior art, must have a reasonable expectation that the modification or combination suggested by the PTO would succeed. *In re Dow*, 5 USPQ2d 1529, 1531-32 (Fed. Cir. 1988).

Third, the prior art, either alone or in combination, must teach or suggest each and every limitation of the rejected claims. *In re Gartside* , 53 USPQ2d 1769 (Fed. Cir. 2000). The teaching or suggestion to make the claimed invention, as well as the reasonable expectation of success, must come from the prior art, not Applicants' disclosure. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991). If *any one* of these criteria are not met, *prima facie* obviousness is not established, and Applicants are *not* required to show new or unanticipated results. *In re Grabiak*, 226 USPQ 870 (Fed. Cir. 1985).

B. No Combination of References Teaches or Suggests Each and Every Element of Amended Claims 5-9

Amended Claim 5 recites a method for producing a polynucleotide that comprises the steps of obtaining a polynucleotide template capable of hybridizing to a gene trapped sequence of SEQ ID NOS:9, 10, 12-14, 16-18, combining the template with an oligonucleotide sequence of about 14 to about 80 bases of a contiguous sequence of one of SEQ ID NOS:9, 10, 12-14, 16-18 and processing the combined oligonucleotide and template. Claims 6-9 depend from Claim 5.

The references cited by the PTO do not teach or suggest a polynucleotide template capable of hybridizing to a gene trapped sequence of SEQ ID NOS:9, 10, 12-14, 16-18 or an oligonucleotide sequence of about 14 to about 80 bases of a contiguous sequence of one of SEQ ID NOS:9, 10, 12-14, 16-18.

For instance, as discussed above, the PTO asserts that AW241926 teaches an oligonucleotide comprising a contiguous stretch of 69, 67 or 43 bases of SEQ ID NO:11.

However, AW241926 does not teach or suggest a polynucleotide template capable of hybridizing to a gene trapped sequence of SEQ ID NOS:9, 10, 12-14, 16-18 or an oligonucleotide sequence of about 14 to about 80 bases of a contiguous sequence of one of SEQ ID NOS:9, 10, 12-14, 16-18.

Also as discussed above, the PTO asserts that AI47895 teaches an oligonucleotide comprising a contiguous stretch of 122 bases of SEQ ID NO:15. However, AW241926 does not teach or suggest a polynucleotide template capable of hybridizing to a gene trapped sequence of SEQ ID NOS:9, 10, 12-14, 16-18 or an oligonucleotide sequence of about 14 to about 80 bases of a contiguous sequence of one of SEQ ID NOS:9, 10, 12-14, 16-18.

Finally, as discussed above, the PTO asserts that Waterson teaches an oligonucleotide comprising a contiguous stretch of 389 bases of SEQ ID NO:11. However, Waterson does not teach or suggest a polynucleotide template capable of hybridizing to a gene trapped sequence of SEQ ID NOS:9, 10, 12-14, 16-18 or an oligonucleotide sequence of about 14 to about 80 bases of a contiguous sequence of one of SEQ ID NOS:9, 10, 12-14, 16-18.

Sambrook does not cure the defects of AW241926, AI47895 or Waterson. Sambrook teaches in vitro amplification of DNA by the polymerase chain reaction. Sambrook does not teach or suggest a polynucleotide template capable of hybridizing to a gene trapped sequence of SEQ ID NOS:9, 10, 12-14, 16-18 or an oligonucleotide sequence of about 14 to about 80 bases of a contiguous sequence of one of SEQ ID NOS:9, 10, 12-14, 16-18.

Since none of AW241926, AI47895, Waterson or Sambrook, alone or in any combination, teaches or suggests a polynucleotide template capable of hybridizing to a gene trapped sequence of SEQ ID NOS:9, 10, 12-14, 16-18 or an oligonucleotide sequence of about 14 to about 80 bases of a contiguous sequence of one of SEQ ID NOS:9, 10, 12-14, 16-18, the PTO's combination of references fails to teach or suggest each and every element of Claims 5-9. As such, the references are not sufficient to establish a *prima facie* case of obviousness Claims 5-9. Applicants respectfully request that the rejection of Claims 5-9 under 35 U.S.C. § 103(a) be withdrawn.

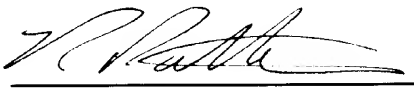
CONCLUSION

Applicants submit that Claims 1 and 3-7 satisfy all of the criteria for patentability and are in condition for allowance. An early indication of the same and passage of Claims 1 and 3-7 to issuance is therefore kindly solicited.

No fees in addition to the extension fee are believed due in connection with this response. However, the Commissioner is authorized to charge all required fees, fees under 37 C.F.R. § 1.17 and all required extension of time fees, or credit any overpayment, to Pennie & Edmonds U.S. Deposit Account No. 16-1150.

Respectfully submitted,

Date: April 24, 2001



42,983

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Exhibit A
Marked Up Version of Amended Claims

3. (Amended) An isolated polynucleotide comprising a contiguous stretch of at least about 60 nucleotides [first disclosed in] of at least one of SEQ ID NOS:[9-503]9, 12-14, 16-18.

5. (Amended) An *in vitro* process for producing a polynucleotide comprising the steps of:

a) obtaining a polynucleotide template encoding a sequence capable of hybridizing to a [GTS] gene trapped sequence of SEQ ID NOS:[9-503]9, 10, 12-14, 16-18;

b) combining said template with a synthetic oligonucleotide sequence of about 14 to about 80 bases in length that comprises a contiguous sequence of at least about 12 nucleotides disclosed in one of SEQ ID NOS:[9-503]9, 10, 12-14, 16-18; and

c) processing the combined oligonucleotide and template preparation such that said oligonucleotide sequence hybridizes to said template in the presence of a DNA polymerase molecule and a sufficient concentration of dNTPs for said oligonucleotide sequence to prime DNA synthesis by said polymerase,

wherein a polynucleotide is produced that encodes at least about 50 contiguous nucleotides first disclosed in one of SEQ ID NOS:[9-503]9, 10, 12-14, 16-18.

Exhibit B
Pending Claims

3. (Amended) An isolated polynucleotide comprising a contiguous stretch of at least about 60 nucleotides of at least one of SEQ ID NOS:9, 12-14, 16-18.

5. (Amended) An *in vitro* process for producing a polynucleotide comprising the steps of:

a) obtaining a polynucleotide template encoding a sequence capable of hybridizing to a gene trapped sequence of SEQ ID NOS:[9-503]9, 10, 12-14, 16-18;

b) combining said template with a synthetic oligonucleotide sequence of about 14 to about 80 bases in length that comprises a contiguous sequence of at least about 12 nucleotides disclosed in one of SEQ ID NOS:9, 10, 12-14, 16-18; and

c) processing the combined oligonucleotide and template preparation such that said oligonucleotide sequence hybridizes to said template in the presence of a DNA polymerase molecule and a sufficient concentration of dNTPs for said oligonucleotide sequence to prime DNA synthesis by said polymerase,

wherein a polynucleotide is produced that encodes at least about 50 contiguous nucleotides first disclosed in one of SEQ ID NOS:9, 10, 12-14, 16-18.

6. The process of Claim 5 wherein said template is mammalian cDNA.

7. The process of Claim 5 wherein said template is mammalian genomic DNA.

8. The process according to Claim 6 wherein said templates are of human origin.

9. The process according to Claim 7 wherein said templates are of human origin.

10. (New) An isolated polynucleotide comprising a contiguous stretch of at least about 20 nucleotides of SEQ ID NO:17.

11. (New) An isolated polynucleotide comprising a contiguous stretch of at least about 30 nucleotides of at least one of SEQ ID NO:9, 13, 14, 16-18.

12. (New) An isolated polynucleotide comprising a contiguous stretch of at least about 40 nucleotides of at least one of SEQ ID NO:9, 12-14, 16-18.

13. (New) An isolated polynucleotide comprising at least one of SEQ ID NOS:9-18.

14. (New) An isolated polynucleotide capable of hybridizing to a polynucleotide of Claim 3, 10, 11 or 12 under high stringency conditions.